

IN THE CLAIMS

The present listing of the claims replaces any prior listing and upon entry of the present amendment, the status of the claims will be as follows:

Claims 1-2 (Cancelled)

3. (Original) The method of claim 1, wherein the bone marrow cells are impaired by the donor having a disorder that impairs naturally occurring angiogenic processes found in normal young healthy individuals

Claims 4-8 (Cancelled)

9. (Original) The method of claim 8, wherein the filtering removes particles larger than from about 300 μ to about 200 μ .

10. (Original) The method of claim 1, wherein the one or more agents are selected from hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

11. (Original) The method of claim 1, wherein the vector is selected from a plasmid vector and an adenoviral vector.

12. (Original) The method of claim 10, wherein the vector is an adenoviral vector.

Claims 13-16 (Cancelled)

17. (Currently Amended) A method for enhancing collateral blood vessel formation in heart or limb muscle tissue of a patient in need thereof, said method comprising:

~~obtaining autologous bone marrow from the patient;~~
~~growing the autologous bone marrow in a suitable medium under suitable culture~~
~~conditions for a period of time sufficient to promote production by the bone marrow of early~~
~~attaching cells;~~

~~transfecting at least a portion of the early attaching cells with an adenovirus vector~~
~~comprising a polynucleotide that encodes one or more agents selected from hypoxia inducing~~
~~factor 1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant~~
~~Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), a fibroblast~~
~~growth factor (FGF), a NOS, and PR39 so as to cause expression of the one or more agents to~~
~~produce conditioned medium; and~~

~~directly administering to~~ injecting into a site of impaired blood flow in heart or limb
muscle tissue of the patient an effective amount of ~~the transfected~~ early attaching cells ~~and/or the~~
~~conditioned medium to enhance collateral blood vessel formation at the site in the patient~~
obtained from autologous bone marrow, which cells have been transfected with an adenoviral
vector comprising a polynucleotide encoding one or more angiogenic factors selected from
hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte
Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-
CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

18. Canceled.

19. (Currently Amended) The method of claim [[18]] 17, wherein the early attaching cells
are marrow-derived stromal cells and the ~~conditioned medium is~~ transfected cells are directly
administered to injected into a site of ischemia in the patient muscle tissue.

Claims 20-23 (Cancelled)

24. (Currently Amended) The method of claim [[23]]47, wherein the period of culturing is from about 3 hours to about 3 days.

25. (Currently Amended) The method of claim [[18]] 17, further comprising filtering bone marrow prior to culturing of the bone marrow to obtain the early attaching cells.

Claims 26 – 28 (Cancelled)

29. (Currently Amended) The method of claim [[18]] 17, wherein the agent is selected from a fibroblast growth factor (FGF), a NOS, and PR39.

30. (Currently Amended) The method of claim [[29]] 17, wherein the agent is selected from FGF-1, FGF-2, FGF-4, and FGF-5.

31. (Currently Amended) The method of claim [[29]] 17, wherein the agent is selected from inducible NOS and endothelial NOS.

32. (Currently Amended) The method of claim [[29]] 17, wherein the agent is PR39.

33. (Cancelled)

34. (Currently Amended) The method of claim [[18]] 17, wherein the method enhances collateral blood vessel formation in the heart or leg muscle tissue.

Claims 35 – 38 (Cancelled)

39. (Currently Amended) A therapeutic composition comprising early attaching cells derived obtained from bone marrow, which cells have been transfected with an adenoviral vector

comprising a polynucleotide that encodes one or more agents selected from hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

40. (Currently Amended) The ~~therapeutic~~ composition of claim 39, further comprising conditioned medium ~~in which the cells have been grown in culture for a time sufficient to allow expression of~~ containing one or more of the agents expressed from the polynucleotide.

41. (Original) The composition of claim 39, wherein the polynucleotide further comprises a transcription regulatory region operatively associated with the polynucleotide.

42. (Original) The composition of claim 39, wherein the transfected cells have been stimulated by exposure to hypoxia.

43. (Currently Amended) The composition of claim 39, further comprising ~~heparin or another~~ an anticoagulant.

44. (Cancelled)

45. (Original) The composition of claim 39, wherein the early attaching cells are marrow-derived stromal cells.

46. (Original) The composition of claim 39, wherein the composition is intended to be injected into a patient having ischemic tissue and the early attaching cells are derived from bone marrow obtained from the patient.

Please add the following new claims:

47. (New) The method of claim 17, further comprising, prior to the injecting, culturing the early attaching cells in a culture medium to produce conditioned medium containing one or more of the agents expressed from the polynucleotides, and wherein the method further comprises injecting the one or more agents in the conditioned medium along with the transfected early attaching cells..

48. (New) The method of claim 17, wherein the injecting is at multiple sites in the muscle tissue.

49. (New) The method of claim 48, wherein the effective amount is about 0.2 to about 0.5 ml of the composition in each of from about 12 to about 25 sites.

In re Application of:
Epstein et al.
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Attorney Docket No.: MEDIV2010-4

No fee is believed due with this submission. In the event that fees are due, please charge our Deposit Account No. 07-1896 appropriately.

Respectfully submitted,

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